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ACUTE PANCREATITIS

CONSIDERED IN RELATION TO THREE CASES OCCURRING  
IN GENERAL PRACTICE.

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## A C U T E   P A N C R E A T I T I S

### CONSIDERED IN RELATION TO THREE CASES OCCURRING IN GENERAL PRACTICE.

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Some experience of general medical practice following upon the initial years of medical training, impresses upon one that the latter period is only a prelude to an unending post-graduate course of study and education; there being at present in hardly any department of medical knowledge anything like finality. But if the general practitioner finds he is still only a student, his opportunities for clinical study present certain advantages over the conditions of study in the wards of a hospital in his earlier days.

Many slowly-developing diseases which are destined to be eventually typical of their kind are seen in embryo by him and are correspondingly difficult to identify; but once suspected, the natural history of the malady in its various stages can be followed from start to finish.

On the other hand, in the case of acute diseases immediately threatening life, he has again the advantage of seeing the case at the very beginning, the symptoms being so urgent that he is summoned at once; and he has thus the chance of observing anything clinically distinctive in the attack apart from its mere severity.

Among such acute diseases, those affecting the abdominal organs form an important class; and among these is Acute Pancreatitis.

It is the object of this paper to discuss some aspects of this affection, in relation to three cases observed during the last five years; and if it be objected that the small number of the cases in question renders unprofitable conclusions drawn from their consideration, it may with some justice be maintained that the disease is apparently not frequently met with; or, if met with not always recognised,- and is accordingly for practical purposes a rare disease; and that it is only by detailed discussion of even isolated cases when identified, that the natural history of such a disease can be followed out and treatment agreed upon.

In the present series the diagnosis was established in all cases; in one by post-mortem examination and in the others by operation during life.

Description of Cases referred to  
with comments.

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CASE I A.B. male 44:

Occupation Publican

He was well known to me prior to his present illness, and definitely alcoholic in his habits.

I was called to see him on April 12th 1905 and found



him in bed suffering from epigastric pain, obviously very severe.

The pain was constant but with paroxysmal exacerbations, and its severity was of a degree altogether exceptional; he showed signs of profound shocks, there was general clammy pallor, and his pulse was hardly to be felt. Temperature 97.4

On inspection of the abdomen there was some limitation of movements on respiration but not pronounced.

On palpation there was no well marked general tenderness in the epigastrium and not any definitely localised tender spot; steady pressure tended to relieve the pain.

The condition appeared to me to be unusually severe biliary colic although I had never from previous experience known him to be harbouring gallstones. A full dose ( $\frac{1}{2}$  grain) of morphia was given hypodermically but to my great surprise failed to give any relief;  $\frac{1}{4}$  grain was therefore given an hour later again without relief; the pain and collapse were unaffected.

On the second day of the illness the condition was the same with certain symptoms added: notably great restlessness and intense thirst. The former was very noticeable, and it was an altogether unusual thing to see a man so profoundly ill - with no pulse at the wrist and collapsed, attempting to get out of bed apparently with the idea of getting relief from pain by change of posture.

Once again morphia failed to relieve, although

repeated until a grain had been given hypodermically in 24 hours, the initial dose being again  $\frac{1}{2}$  grain. There was considerable nausea and occasionally small quantities of bilious vomit; but vomiting was at no time a striking symptom.

Third day: there was now to be observed some circumscribed swelling in the epigastric region above the umbilicus. There was complete constipation, but flatus could be passed and there were not present the signs of intestinal obstruction.

By now it was borne in upon me that I was witnessing a combination of clinical symptoms which I had never previously set eyes upon and constituting to me a new disease.\*

Fourth day: The severity of the symptoms as regards pain and collapse had slightly abated: the pulse returned at <sup>the</sup> wrist; feeble, rapid, (112) and of low tension. Temperature 98° 8. Still no action of the bowels.

Fifth day and afterwards: Improvement was gradually maintained, the bowels were moved on the 7th day - a large greenish slimy evacuation.

On the tenth day he was able to be out of bed and although very weak was comparatively well.

This initial attack lasted from the 12th to 21st April.

\* Cf. Halsted: Johns Hop. Hosp. Bull. 1901 Nos 121, 2, 3.

Subsequent history from April 20th to June 21st.

After April 20th he gradually recovered strength and resumed his ordinary occupation. The only persisting symptom which I noted was "pain in the back" brought on by stooping while working in the garden; the pain was in the lower dorsal region, and not acute, - more of a dull ache, and always brought on by continuous stooping. (This symptom I shall refer to again).

On June 20th I was again summoned and found him in acute pain and collapse which lasted for 24 hours and terminated fatally, all palliative treatment being again unavailing; the symptoms were identical with those occurring on April 12th.

Post Mortem Examination.

The abdomen only was investigated, the examination being conducted under difficulties inseparable from such operations carried out on the floor of a private bedroom. On opening the abdomen there was no general peritonitis. The liver showed signs of the early fatty stage of cirrhosis. The gall-bladder contained no gall-stones, nor were any to be found in the cystic and common ducts. The fat in the root of the mesentery and omentum was here and there converted into soft lumps of the consistency of butter. The lesser sac of the peritoneum was distended and full of turbid chocolate-coloured fluid; and floating free in this fluid were dark lumps of old



and recent blood-clot, and tougher masses consisting of gangrenous pancreatic sequestra.

The pancreas was disorganised: parts of it were soft and pulpy, other parts tough and indurated; there were areas showing old and recent haemorrhage.

#### Microscopic Examination of the pancreas.

Difficulty was experienced in securing a portion of the gland for microscopic examination which was not hopelessly necrotic. The annexed micro-photograph shows however early and later inflammatory changes: the former evidenced by small round-celled infiltration and the latter by overgrowth of fibrous tissue.

Crystals of haematin are distributed throughout the specimen.

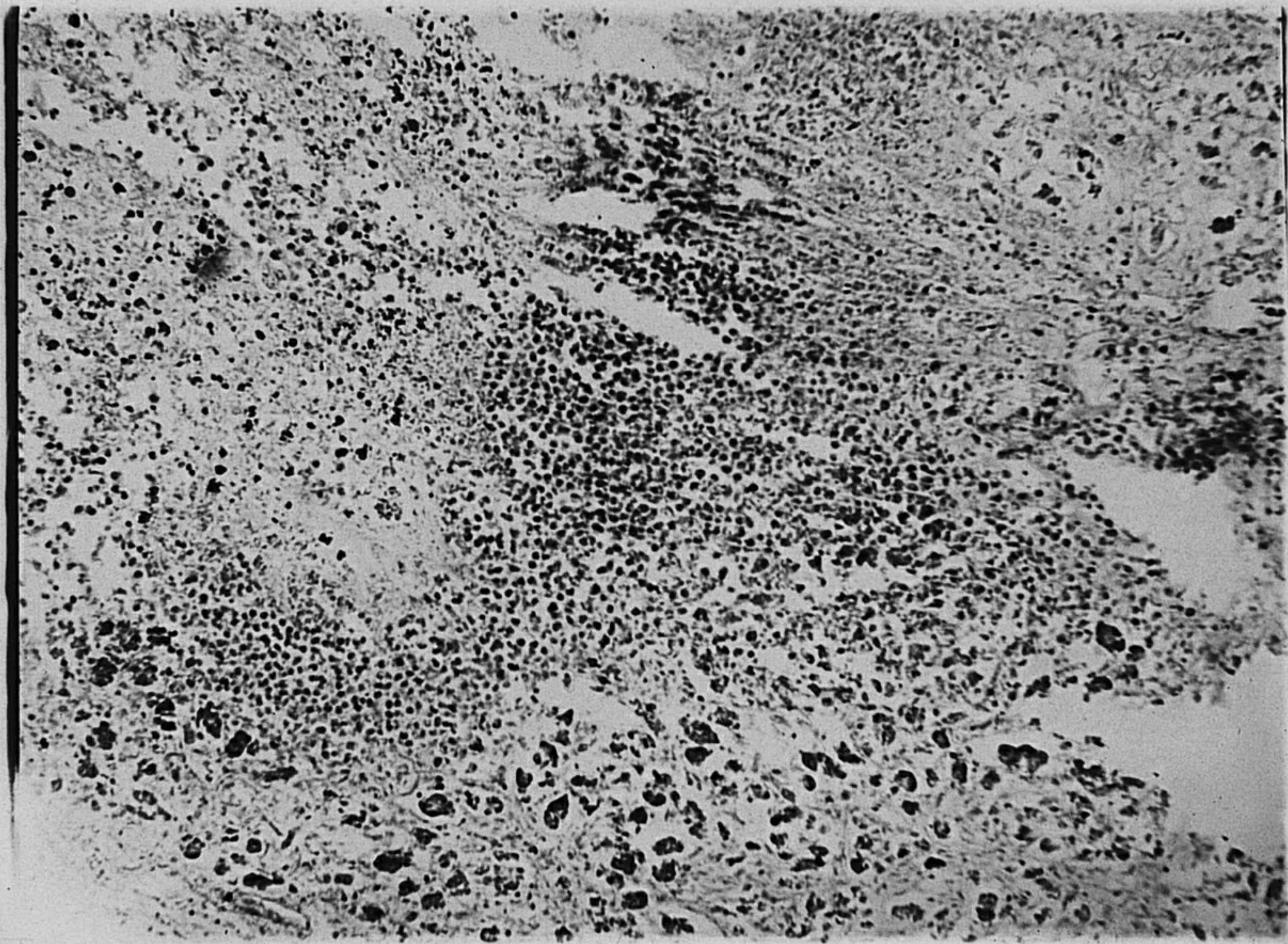
The glandular elements show great disintegration part of which may have been due to post-mortem changes.

#### COMMENTS ON CASE I.

This case interested me greatly the disease being to me entirely new. I had never previously met with a case presenting the same clinical picture\*, and was at the outset unacquainted with the available literature dealing with the condition. Hence the original erroneous diagnosis of gall-stones. Subsequent study of the subject has shown me that others have made the same mistake for the same reasons, viz:-lack of experience of

\* Cf. Halsey: op. cit.







actual cases and ignorance of the literature dealing with such. The salient features observed during the early days of A.B's. illness were:

- (1) The intensity of the epigastric pain and the conspicuous failure of large doses of morphia to relieve it.
  - (2) The profound and continued depression of the circulation, never previously met with in my experience to such an extent, except in a moribund person.
  - (3) The combination with (2) of active motor restlessness and mental clearness.
  - (4) The absence of clear evidence either from signs observed or from knowledge of previous history of ordinary abdominal emergency-lesions, e.g. perforated gastric or duodenal ulcer, fulminating appendicitis, acute cholecystitis, acute intestinal obstruction.
  - (5) The temporary recovery - practically without treatment - from what looked like a mortal illness.
  - (6) The unusual post-mortem appearances.
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CASE II. C.D. male.

Occupation: Gardener.

A month after the death of Case I. while the impressions gained were fresh in my memory, I saw Case II in consultation with a colleague who was in charge of the case.

The man had hitherto been robust but there was a

clear history of alcoholic excess. On a Sunday evening in July 1905 at 6 p.m. he was quite well; at 8 *p.m.* he was seized with intense abdominal pain. I saw him on the Monday and helped to carry him from his bed to a stretcher on which he was removed to the Cottage Hospital. The provisional diagnosis made by my colleague was that he was suffering from perforative peritonitis demanding laparotomy; the general signs of collapse were well-marked. I remarked that the case reminded me strongly of Case I.

Laparotomy was performed the same evening and subjoined are the notes of the surgeon who carried out the operation.

" The abdomen was opened through the right rectus muscle: a few ounces of blood-stained fluid escaped; the intestines were injected and slightly distended. There was ~~ondema~~ edema of the cellular tissue in the region of the pancreas, and areas of fat-necrosis in the omentum and mesentery." *No further operative procedure was carried out.*  
*specimens*  
 The abdomen was <sup>specimens</sup> closed without drainage.

Subsequent history: The effect of the operation was to produce at once relief of symptoms and recovery was rapid and complete.

A few weeks ago I sought out the man and found him in apparent vigorous health pursuing daily his occupation as gardener. During the last five years he had two days' illness: abdominal pain for which he never sought medical



aid. I secured a specimen of his urine which from recent research (to be further discussed) is of interest. The subjoined report by Dr. P.J. Cammidge shows that it exhibits the "pancreatic reaction."

### REPORT

Dr. Dick's case;- Report on a specimen of urine  
received March 23<sup>rd</sup> 1910.

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Reaction.....	acid
Sp.Gr.....	1.006
Albumen.....	nil, some nucleo-proteid
Sugar.....	Fehling. - no reduction
	Phenylhydrazin.- some small ro-
	settes of crystals
	Bial's reagent.- slight green,
	specroscopical examination
	shows two faint bands in the
	red.
Acetone.....	nil
Aceto-acetic acid.....	nil
Indican.....	nil
Bile.....	nil
Urobilin.....	nil
Blood.....	nil
Urea.....	subnormal, 0.71%
Chlorides.....	sub-normal, 0.26%
Phosphates.....	sub-normal, 0.05%
Microscopically.....	some uric acid crystals, a few
	small calcium oxalate
	crystals, some yeast cells.
Pancreatic reaction....	C.- a few fine crystals, soluble
	in 5-10 seconds.

Although this specimen contains no appreciable quantity of reducing sugar the results of Bial's reaction and the phenylhydrazin test suggest that it contains a trace of pentose or a marked excess of glycuronic acid. The absence of any marked reaction for indican, with which the glycuronic acid is most commonly combined, is however against the latter. The results of the pancreatic reaction point to there being some slight active degenerative changes in the pancreas at the present time. The absence of bile pigment shows that there is no obstruction to the free flow of bile into the intestine and the negative result of the urobilin reaction is against there being any serious interference with the functions of the liver or cholangitis

such as usually accompany the presence of floating gallstones in the common bile duct. The presence of only traces of indican is against there being any abnormal putrefactive changes in the contents of the upper part of the intestines with catarrh of the walls to which the pancreatitis might be secondary. The presence of small calcium oxalate crystals in the centrifuged deposit tends to confirm the diagnosis of chronic pancreatitis and suggests that the condition is of some standing.

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### COMMENTS ON CASE II.

(1) As in Case I we have here the initial intense pain in the upper abdomen with an absence of facts in the previous history pointing to any obvious cause for it e.g. gastric or duodenal ulcer, cholecystitis or biliary colic.

(2) Complete relief and apparent cure following laparotomy.

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### CASE III. Lady aet. 45 in good circumstances.

This case was under the care of my partner and was seen by me along with him during the course of her illness which terminated fatally in 48 hours.

The following notes represent my partner's previous knowledge of her medical history since she came under his care and our joint observation of her last illness. She was a particularly vigorous woman, physically and mentally. Her only notable malady during the past 6 years was oxaluria



which produced symptoms of slight renal colic and yielded easily to general treatment largely dietetic.

The history of oxaluria is significant in this case in view of Cammidge's researches.

One morning on waking she had slight pain which she put down to indigestion. She went to do some shopping and while so engaged was suddenly seized with severe abdominal pain and had to return home; on the way she vomited. On examination at midday she looked ill and complained of severe pain in the epigastrium also over the lower part of the sternum and along each parasternal line. There was no marked rigidity of the recti; pressure did not increase or diminish the pain; morphia was given on the supposition that she was suffering from biliary colic; it did not produce relief. In the evening her condition was unaltered; the pain which was kept under by chloroform was now also felt in the back - lower dorsal region, the pulse was just over 100, and of poor quality; the temperature was normal; there was no evidence of intestinal obstruction; during the night the general condition got worse and in the morning a surgeon was summoned. By this time there was dulness on percussion in the left epigastric region and left hypochondrium; there was also a slight degree of general cyanosis.\* The surgeon decided to perform laparotomy since although the clinical signs were highly suggestive of Acute Pancreatitis it was difficult to exclude perforated gastric ulcer.

\* Halsted (op.cit.) lays stress on this symptom; it appears to be the direct result of the circulatory depression.

Surgeon's notes of the operation:

"The lesser peritoneal sac was full of blood-stained fluid; there was much fat necrosis.

There was no evidence of any gall-bladder complication; and no sign of any gall-stones in any part of the bile ducts from beginning to end.

The Pancreas was a soft pultaceous mass, and there was no sign of tension within its capsule. The appearance suggested more of a sloughing condition than anything else.

A drainage tube was passed down to the site of the pancreas and the abdomen was closed."

The condition of the patient after operation showed no improvement; cyanosis became more marked and she gradually sank and died from cardiac failure retaining consciousness till shortly before death; no post-mortem examination was available.

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#### COMMENTS ON CASE III.

- (1) The onset of the illness was rather less sudden than in cases I and II.
  - (2) Cyanosis was a well marked symptom.(c.f. Halsted's case)
  - (3) Laparotomy and drainage afforded no relief
  - (4) There was a history of oxaluria. This was the only fact of positive help in pointing to a diagnosis, so far as the previous history was concerned.
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<sup>E</sup>ETIOLOGY & PATHOLOGY  
of  
ACUTE PANCREATITIS.

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Preliminary considerations:- Before entering upon this discussion it may be profitable to try and arrive at some clear notion of what the disease essentially consists in considered clinically; and for this purpose the above 3 cases are sufficient. There is to my mind, in the literature dealing with the subject far too great a tendency to try and "bring the disease into line" with other acute inflammatory affections, such as e.g. appendicitis and perforating gastric ulcer.

Now to put it briefly the common "abdominal catastrophes" tend to be fatal because they are infective, i.e. organismal and speedily lead to general peritonitis: and since in the above three cases general peritonitis was absent, it is evident that the disease under consideration cannot completely be brought into line" with the ordinary acute inflammatory abdominal conditions; and attempts to do so in defiance of obvious clinical discrepancies with the latter are unscientific, and from the point of view of diagnosis and treatment they are in practice mischievous.

On the subject of Acute Pancreatitis, Fitz was a pioneer.\* His monograph\* ought to have focussed the attention

\* New York Med. Record: 1889, xxv 197, 225, 253

of all practitioners on the disease; and it is astounding that although Fitz wrote in 1889 it is only during the last decade that the subject has aroused, in this country at least, much active interest and investigation. (But it is characteristic of the average Briton to regard as non-existent things which are outside his experience).

Nevertheless a study of Fitz's paper makes me think that he was not free from the modern tendency to try and "bring the disease into line" at the expense of obscuring its conspicuously "outré" character. (<sup>cf.</sup> Halsted) Under Diagnosis he says "The symptoms are essentially those of a peritonitis beginning in the epigastrium and occurring suddenly during ordinary health without obvious cause." ~~✗~~

This does not seem to cover the ground so far as the above 3 cases are concerned.

In them the early symptoms were:-

- (a) Hyperacute epigastric pain without that notable rigidity and tenderness characteristic of peritonitis.
- (b) Profound circulatory depression amounting to that seen in surgical "shock" and continued for a period much in excess of that approached in any ordinary abdominal catastrophe.

I could imagine (b) as being comparable clinically to the effects of snake-poison.

The object of the preceding remarks is to make clear that however constantly the symptoms and the pathological appearances, ante-mortem and post-mortem, are partly those of an acute inflammation of the pancreas, the

disease consists very largely in the remote effects of this process without general peritonitis; and this ought to be borne in mind when discussing aetiology and pathology.

AETIOLOGY:- The main causes discussed in the literature are:-

- (1) The effects of gall-stones.
- (2) Infection from the duodenum.
- (3) Haemorrhage.

Other causes such as embolism and infarction, trauma, metastasis in mumps, it is not proposed to discuss here.

(1) The effects of gall-stones: A study of the literature dealing with Acute Pancreatitis shows that there is a strong consensus of opinion that gall-stones are a pre-eminent mechanical factor in producing the disease. Consideration of the 3 cases described above in all of which gall-stones were absent, shows I think conclusively that however potent a cause cholelithiasis may be in producing many cases of Acute Pancreatitis, the latter cannot be said to be essentially dependent on the presence of gall-stones or their mechanical effects.

The case of Halsted<sup>1</sup> investigated by Opie<sup>2</sup> is in this connection a classic.

Opie found on post-mortem examination that there was present in the Ampulla of Vater a gall-stone partially filling it so as to prevent bile from flowing

<sup>1</sup>Halsted: *op. cit.*

<sup>2</sup>Opie: *Bull. Johns Hop. Hosp.* 1901, xii, 182.



into the duodenum, but not of size sufficient to completely fill the ampulla; so that the bile failing to flow into the duodenum was diverted past the calculus into the Duct of Wirsung; the common bile duct and the Duct of Wirsung being converted into a continuous channel.

Evidence of the bile having actually reached the Duct of Wirsung was found, the walls of the latter being bile-stained.

Opie therefore concluded that acute Pancreatitis had been caused in this case by "retrojection" of bile along the duct of Wirsung owing to the mechanical conditions present due to the gall-stone partially filling the Ampulla of Vater whereby the bile was diverted from the common bile duct along the Duct of Wirsung.

~~Opie~~ <sup>Flexner</sup> subsequently proved by actual experiment on dogs that injection of bile into the Duct of Wirsung produced in them Acute Pancreatitis.\* Opie's case, however interesting, is not to my mind convincing for the following theoretical reasons.

It is admitted that gall-stones are exceedingly common and in many cases they are frequently passed into the duodenum and can be recovered from the faeces. It must surely happen that whenever a gall-stone is passing into the duodenum through the Ampulla of Vater a stage in its transit must be reached - and the process might be arrested for a time at that stage - when it produces the conditions discovered in Opie's case viz;- of only partially filling the Ampulla and

\* Flexner: Journal of Experimental Medicine: Jan. 1906 ~~Vol~~ 167.

thus converting the common bile duct and Duct of Wirsung into a continuous channel.

Retrojection of bile might therefore occur in every case of gall-stones when a stone was being passed into the duodenum, even if the necessary conditions as affecting the junction of the common bile duct and the Duct of Wirsung only lasted for a few minutes.

(2) Infection from the duodenum.

It is suggested that the infection arises because of the existence in the duodenum of Chronic Catarrh.

In this connection may be mentioned the point of alcoholism; in two of the above cases this was well marked and both the patients suffered from gastro-duodenal catarrh largely no doubt due to alcohol.

When however one considers the enormous number of people who suffer from gastro-duodenal catarrh, alcoholic or otherwise, and the few who develop Acute Pancreatitis it is hard to see how the former can be a really potent factor in producing the disease.

The presence of a chronic inflammatory condition in the duodenum would no doubt favour bacterial invasion of the duct of Wirsung; but in this connection it is noteworthy that many cases have been recorded in which the exudation in the neighbourhood of the affected pancreas was sterile. \*

\* Stewart's cases *Ann. Surg.* 1906. 723.

\* Truhant: *Pankreas-Pathologie*; Wiesbaden 1902.

(3) Haemorrhage.

The association of haemorrhage into and around the pancreas is in many cases of acute Pancreatitis so notable that it has been regarded as a cause of the disease. This matter will be discussed under Pathology.

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P A T H O L O G Y

Under this head may be discussed-

- (1) The appearances of the Pancreas as regards inflammation.
- (2) Haemorrhage.
- (3) Fat-necrosis.
- (4) The Urine.
- (5) The Cause of Death.

(1) The pancreas shows different conditions of inflammation according as it is observed early in the course of the disease, during laparotomy, or later post-mortem. It may be simply enlarged in all or most of *its* dimensions with some tenseness of its capsule and oedema of the surrounding cellular tissue (vide Surgeon's notes Case II); if this condition is unrelieved the tension leads to disorganisation of the parenchyma of the organ (vide Surgeon's notes, Case III).



Microscopic examination of the organ in the early inflammatory condition shows some small-celled infiltration and early vacuolisation of the parenchymatous cells. There is a preponderance of evidence against this early inflammatory condition being due to organisms; the advent of the latter is a late event in the course of the disease: "it is now agreed by almost all writers on the subject that the bacteria isolated---have no aetiological connection with the lesion and are only present through secondary invasion of the injured tissues."<sup>1</sup>

This is a significant conclusion against the aetiological importance of infection from a chronically catarrhal duodenum. The later extreme results of the inflammatory process are the production of necrosis and sometimes gangrene of the pancreas; Case I is typical of the progressive inflammatory process ending in gangrene. In both the early and late stages of inflammation haemorrhage may be present and obvious.

Suppuration is not a feature of the disease as in ordinary inflammatory infections.

Fitz however thought there were cases of Suppurative Pancreatitis, which ran a course similar to Acute Pancreatitis beginning with equal suddenness but not so rapidly fatal, and more rarely associated with fat-necrosis.<sup>2</sup>

He also collected 22 cases of Suppurative Pancreatitis which he regarded as cases of Acute

<sup>1</sup> *The Pancreas, its Surgery & pathology by Mayo, Robson and P.J. Cumming* p. 142.

<sup>2</sup> Fitz : *op. cit.*

Pancreatitis showing a stage of Suppuration. But it is difficult to estimate the value of these cases most of which were reported many years before Acute Pancreatitis was recognised clinically and before fat-necrosis was described.

It may be definitely stated that in Acute Pancreatitis suppuration is not a notable feature judging from the cases reported since the publication of Fitz's monograph.

(2) Haemorrhage. The occurrence of haemorrhage into the pancreas and surrounding tissues is well marked in many cases and has been regarded as of prime importance in producing the disease.

Fitz regarded it as directly causative in certain cases hence his title Acute "Haemorrhagic" Pancreatitis;<sup>1</sup> but in other cases he regarded the haemorrhage as secondary to the inflammation and his reasons for differentiating between the two classes are not forthcoming.

Mayo Robson<sup>2</sup> regards as (a) ultra-acute the cases "in which haemorrhage precedes inflammation and the bleeding is profuse both inside and outside the gland" and as (b) Acute the cases "in which inflammation precedes haemorrhage which is less profuse and is distributed in patches throughout the gland."

Here again we are left without clear guidance as to the above being a distinction capable of demonstration

<sup>1</sup> Fitz: *op. cit.*

<sup>2</sup> Mayo Robson & Cannon: *op. cit.* p. 363.

and proof. The difficulty can only be cleared up when, in cases of acute Pancreatitis the immediate cause of the bleeding is discovered. Bleeding into the Pancreas is known to occur from a variety of causes, e.g. trauma, heart disease, altered blood conditions as in the acute infectious diseases, scurvy, atheroma; and in these conditions the haemorrhage is not necessarily associated with Acute Pancreatitis.

My impression is that the importance of the occurrence of haemorrhage in Acute Pancreatitis is much exaggerated probably because when present in the organ examined it is so obvious and easy to recognise. It plays no important part in the symptomatology of the affection except possibly in aggravating the pain if repeated sudden haemorrhages occur; it may be very small in amount while the symptoms of pain and shock are intense.

In fact there is nothing in the clinical picture of the disease suggesting that haemorrhage is a potent factor in producing its ultimate clearly defined aspect; and cases such as I and III above occur which are typical of early Acute Pancreatitis and in the one haemorrhage may be present and in the other absent, or trifling.

On various grounds it seems to me that in the light of our present knowledge of the pathology of Acute Pancreatitis it would be better to drop the term "haemorrhagic," and further that in the absence of a



definitely established explanation of the cause of the haemorrhage it is on theoretical grounds and by analogy most probably a result and not a cause of the disease.

(3) Fat-Necrosis. This condition is by far the most striking pathological phenomenon of the disease under consideration.

Fat-necrosis was first described by Balser<sup>1</sup> in 1882; and later it was proved by Langerhans<sup>2</sup> that the areas of necrosis were produced by the splitting of fat into fatty acids and glycerine; the latter is absorbed and the former combine with calcium to form soap.

The appearances produced by fat-necrosis are quite characteristic and were at once recognisable in all the above three cases; in Case I the condition was present to an extreme degree, so that large masses of material of the consistency of butter were produced in the root of the mesentery.

Fat-necrosis has been frequently produced experimentally. It can be brought about by any agency liberating the pancreatic secretion from its natural situation in the gland; and there is at present no clear evidence of its being produced by any other substance than the pancreatic secretion; but there is a probability that the lipase contained in the latter requires the co-operation of trypsin to cause preliminary cell-death before the fat-splitting action of the former is brought into play.

The splitting of fat is thus a consequence, and not a

1 Balser: *Arch. f. path. Anat.* 1882, *xc*, 520.

*Verhandl. d. XI. Cong. f. innere Med.* 1892, *S* 450.

2 Langerhans: *Berliner klin. Wochenschr.* 1889, *S* 1114; *Arch. path. Anat.* 1890 *LXXII* 252.

cause, of the necrosis. /

The conditions for producing fat-necrosis are constantly present in Acute Pancreatitis; and if in addition the clinical symptoms of Acute Pancreatitis are present then the recognition of fat-necrosis is practically pathognomonic of the disease.

But cases have been recorded showing disseminated fat-necrosis without evidence of accompanying pancreatic disease.<sup>1</sup> These cases are hard to explain; but it may well be that the pancreatic secretion is still the causative agent, the morbid affection of the pancreas whereby its secretion is abnormally liberated being in these cases unaccompanied by any recognisable changes in the organ.

It is, I believe, on the lines of investigating the absolute initiation of the process whereby the pancreatic ferments are abnormally liberated, that the elucidation of all the phenomena, pathological and clinical, is to be eventually achieved.

(4) The Urine. The chemical reaction present in fat-necrosis resulting in the production of glycerine led Cammidge to make experiments directed to the possibility of detecting free glycerine in the blood from cases of supposed pancreatic disease.\* This line of investigation was abandoned; but as a result of continued experiment Cammidge found that the urine in cases of suspected pancreatic disease gave evidence on

<sup>1</sup> *Hills: Chemical Pathology 1907 p. 321-324.*

<sup>2</sup> *Jawcett: Lancet Dec 1906 p. 1512.*

*Sawyer: Lancet Jan 1907 p. 158*

\* *Opie found evidence of the presence in urine of a fat-splitting ferment, in one case. Dis. of Pancreas, 322.*

analysis of the presence of a "sugar-complex probably a nucleoglycoproteid which on hydrolysis with hydrochloric acid gives rise to a substance having the reactions of a pentose and the typical crystals obtained in the reaction are pentosazone crystals".<sup>1</sup> These crystals obtained by the reaction between phenylhydrazin and the nucleoglycoproteid are microscopically "long, light yellow, flexible, and hair-like, arranged in sheaves which when irrigated with 33% sulphuric acid melt away and disappear in ten to fifteen seconds after the acid first touches them."<sup>\*</sup> Cammidge excluded the possibility of the "pancreatic reaction" depending on metabolic changes due to abolition of the function of the gland by experiments carried out on pancreatectomised dogs; in the latter the reaction was not obtained even although present previous to pancreatectomy while the gland was in a condition of acute inflammation artificially produced.<sup>2</sup>

Case II of the above series is of interest in still exhibiting the pancreatic reaction 5 years after the original illness.

Cammidge's pancreatic reaction is of value as a diagnostic and of great chemical interest, but its usefulness in cases of Acute Pancreatitis is somewhat limited since the chemical investigation required is elaborate and demands a high degree of technique if the results are to be reliable.

At present however a positive "pancreatic reaction"

<sup>1</sup> Proc. Roy. Soc. 1910 - Cammidge and Simon.

<sup>2</sup> Cammidge & Simon: *op. cit.*

<sup>\*</sup> Cammidge: *Med. Chir. Trans.* Vol. 89 "An Improved method of Performing the "Pancreatic Reaction" in the Urine. (1906)



in a sample of urine is strong presumptive evidence of the existence of some form of pancreatic disease.

(5) The Cause of Death. This is still largely a matter of pure speculation. It may be that in some cases death is produced very early and suddenly by "shock" causing reflex cardiac inhibition: the rapidly produced circulatory depression amounting to a state of syncope combined with the intense pain (as in Case I) would make such a mechanism possible.

It is possible that the inflammatory process by producing local tension may cause severe shock reflexly through the solar plexus, the clinical signs being strikingly similar to those produced by a blow on the epigastrium or testicles. But when death is delayed for a few days the possibility of a toxic condition being responsible is strongly suggested.

Doberauer's experiments<sup>x</sup> led him to believe that death was caused by the absorption of poison produced in the inflamed gland. He produced Acute Pancreatitis in dogs by ligature and division of the pancreas; and the insertion into other animals of portions of the inflamed pancreas produced in them the same disease. But he found that the effects of ligature and division of the pancreas could be prevented by previous repeated small doses of inflamed pancreas.

As a result of these experiments he concluded that immunity could thus be established "not to pancreatic

<sup>x</sup> Doberauer quoted Ann. Surg. 1906, 789.

substance but to poison contained in the inflamed organ."

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### SYMPTOMATOLOGY, DIAGNOSIS & TREATMENT.

SYMPTOMS: Sudden deep-seated epigastric pain rapidly attaining a sustained degree of severity quite extraordinary is the initial symptom.

The agony is so intense that it is difficult to obtain from the sufferer reliable information as to its characters; but if it is referred (as in all three cases above), to the back (lower dorsal region), this is an important diagnostic point on which, in my opinion, sufficient stress is not laid; the pain may radiate upwards towards the thorax. The pain having rapidly become intense is maintained so continuously; there is no marked remission as in the various forms of colic, although it tends to be paroxysmal. General symptoms of collapse are present almost from the outset evinced by great circulatory depression, the skin being pale and clammy and later cyanotic; pupils semi-dilated, pulse difficult to feel, rapid, of very low tension, and eventually altogether absent at the wrist for hours on end (vide Case I.). On inspection of the abdomen there may be limitation of the respiratory movements, but this is not a striking symptom. On palpation there is an absence of the two cardinal physical signs of peritonitis viz: rigidity and tenderness; on the contrary

pressure tends to relieve the pain and was in Case I constantly applied by the patient himself; constipation is usually well marked but flatus can be passed. Vomiting is in my experience not a notable feature. Intense thirst and great restlessness may be present; the mental condition is quite clear and the patient is miserably aware of the desperate nature of his malady. After the first 24 hours other physical signs may be developed; there may be localised epigastric swelling and perhaps dulness on percussion extending into the left hypochondrium. If the patient survive for more than 2 or 3 days the pain tends to become more widely diffused but is less intense; there is still however an absence of the classical signs of general peritonitis.

Examination of the urine if this can be carried out may show the "pancreatic reaction", and oxaluria is frequently present.

DIAGNOSIS: the diagnosis though difficult ought to be possible in well-marked cases such as the above. The first essential towards making a diagnosis is to bear in mind the rule laid down by Fitz more than 20 years ago. "Acute pancreatitis is to be suspected when a previously healthy person, or sufferer from occasional attacks of indigestion, is suddenly seized with violent pains in the epigastrium followed by vomiting and collapse, and, in the course of 24 hours, by a circumscribed epigastric swelling, tympanitic or resistant, with slight rise of

\* Fitz: op. cit.



temperature." The application of the above rule implies some knowledge of the previous history of the patient, - not always possessed by the medical attendant and hard to elicit from the agonized patient. If however the previous history is known it is of great value as an aid to a differential diagnosis.

In the entire absence of knowledge of the previous history it is extremely difficult to make a positive diagnosis of Acute Pancreatitis within the first 24 hours; the main reason for this being that it is almost impossible to exclude with certainty perforating gastric or duodenal ulcer.

In such circumstances the presence (ascertained as rapidly as possible) of the "Pancreatic reaction" is of great value.

But I would suggest that in the latter serious gastric or duodenal conditions which of course demand immediate laparotomy, the pain and general constitutional symptoms are much less severe and sustained, and the signs of localised peritonitis (tenderness and rigidity on palpation) are well-marked, which I do not believe they are in cases of Acute Pancreatitis.

If the patient is obviously well nourished this is against the probability of gastric or duodenal perforation.

When, however, the previous history is known or can be ascertained, it is of great help in excluding the probability of perforating gastric or duodenal ulcer.

Other affections to be excluded are:-

- (1) Intestinal Obstruction.
- (2) Irritant poisoning.
- (3) Biliary Colic and Cholecystitis.
- (4) Fulminating Appendicitis.
- (5) Tabetic gastric crisis.

(1) Intestinal Obstruction: It is rare to find intestinal obstruction with the early symptoms referred clearly to the epigastrium. Vomiting is a conspicuous early symptom in obstruction high up in the gut, and may be quite inconspicuous in Acute Pancreatitis. Hourly observation of the progress of the disease fails to show the development of complete obstruction to the passage of the contents of the bowel; and general abdominal distension and signs of general peritonitis are not present. Moreover the severe constitutional symptoms rapidly produced, are not observed to anything like the same degree in any form of intestinal obstruction in its early stages.

(2). Irritant poisoning. Is to be excluded by the absence of local caustic action and of evidence of poison having been taken accidentally or suicidally.

(3). Biliary colic and cholecystitis. In biliary colic there will probably be a history of previous attacks; the pain is typical in its character and distribution, and is accompanied by definite remissions

and the general constitutional symptoms are much less severe.

In cholecystitis the distended gall-bladder can usually be felt and there are signs over it of localised peritonitis.

(4) Fulminating Appendicitis. In Fulminating Appendicitis the pain is at first around the umbilicus and is soon referred to the region of the appendix; there are early the signs of commencing general peritonitis and often at the beginning a considerable rise of temperature.

(5) Tabetic Gastric Crisis; can be excluded by failure to find the signs of Tabes.

PROGNOSIS: the majority of cases are fatal within 2 or 3 days if not treated surgically; and the mortality under operative treatment is high.

"Of 59 reported cases of operation during the acute stage 23 recovered." (*Mayo-Robson & Cumming op. cit. p. 404*).

TREATMENT. This is bound to be unsatisfactory so long as the essential nature of the disease and of its remoter effects on the economy is unknown, which it is at present. Palliative treatment directed to the relief of pain is imperative. Morphia, however, is surprisingly inefficient, probably because the circulation being so profoundly depressed the drug is much too slowly absorbed. Inhalation of chloroform gave some relief in Case III.



Stimulants externally and internally are equally disappointing in relieving the symptoms of collapse. No specific medical treatment is at present available.

Under the head of operative treatment may be discussed -

- (a) Indications for operation.
- (b) Rationale of operation when decided upon.
- (c) Actual operative procedures.

(a) It must at once be laid down that if perforating ulcer cannot be excluded,- and many surgeons hold that this can never with certainty be done - laparotomy is at once demanded; the possibility of leaving unrelieved such a certainly fatal condition as perforative peritonitis must always be before the surgeon.

If however operation is decided upon having in view the probability of the disease being Acute Pancreatitis then one must ask what is

(b) the Rationale of operation: the reply of the surgeon frequently is that he must operate on the same lines as for e.g. acute appendicitis; i.e. to remove a source of infection or its consequences.

But if, as seems well-established, acute Pancreatitis is in its early stages not a septic disease, operation cannot be justified on such grounds. In the early stages of the disease the sole object of operation should be to relieve the tension inside the capsule of the pancreas which if unrelieved leads to necrosis of the organ in whole or in part with ultimately fatal results.

Cases II and III above are instructive surgically.

In Case II the presumption is that merely opening the abdomen so affected the local pancreatic conditions, by relieving tension, that resolution occurred instead of necrosis.

In Case III where the operation was carried farther and the actual condition of the pancreas was investigated, the stage of intra-capsular tension was past and necrosis was already established; and it is hard to see how operation could here be of the slightest service, - certainly not by evacuating septic material of the presence of which there was no evidence.

In the rarely-occurring late gangrenous condition as in Case I operation should include free drainage of what is by then practically a septic lesser peritoneal cavity.

(c) Actual operative procedures: As regards an anaesthetic local anaesthesia has been advocated. Personally I should always prefer to give a general anaesthetic.

The abdomen is opened by an incision above the umbilicus in the middle line; if acute Pancreatitis is present, fat-necrosis will be at once noted.

The condition of the pancreas should be investigated by opening the lesser sac through the gastro-colicomentum.

If there are signs of tension within the capsule this should be relieved by free incision; haemorrhage may be free and must be controlled by direct pressure applied by gauze plugs.

The abdomen should then be rapidly closed a drainage tube being previously passed down to the pancreas. In the later gangrenous cases where drainage of the lesser sac is required, this can be best attained by using a posterior incision recommended by Mayo Robson <sup>in</sup> the left costo-vertebral angle, which insures adequate vertical drainage of the large abscess cavity. In addition the intravenous injection of warm normal saline solution should be employed.

*Mayo Robson & Cannon Op. ut. p. 401*

### S U M M A R Y.

Acute Pancreatitis, is a rare disease, and apt to be mistaken for other affections, unless the possibility of its occurrence is kept in mind when dealing with any acute abdominal illness. It is probable however that cases occur oftener than the available statis-

tics indicate. *Recorded cases of fatal biliary colic, and cases of recovery from perforating ulcer without operation, were very probably in many instances really cases of Acute Pancreatitis.*

The Aetiology and Pathology are not as yet fully understood, especially as regards the production of the very grave constitutional effects which tend to be early fatal. In a large proportion of recorded



cases gall-stones were present, and may have been of importance in bringing about conditions favourable to the production of the disease; but typical cases may arise without the presence of gall-stones.

Fat-necrosis is the most striking of all the pathological conditions exhibited. Cammidge's "pancreatic-reaction" is probably invariably present.

The Symptomatology in typical cases is very clearly defined: the symptoms, local and general, are marked by an unusual degree of severity.

The Diagnosis, presents difficulty if it is to be made early, chiefly because it is hard to exclude with certainty commencing perforative peritonitis. If exploratory laparotomy is carried out, the presence of fat-necrosis taken in conjunction with the clinical symptoms and the presence of the "pancreatic-reaction" is pathognomonic.

The Prognosis, in the light of the present available lines of treatment is bad.

The Treatment is not yet scientifically based on full knowledge of the aetiology and pathology, and is to that extent unsatisfactory. Failing the acquisition of further knowledge of the subject revealing specific medical treatment, the best results are probably to be attained by early operation on the lines above indicated.